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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/138,735	08/24/98	PARANHOS-BACCALA G	WPB-36400B

EXAMINER

HM22/0924

GRASER, T

ART UNIT	PAPER NUMBER
1645	14

DATE MAILED: 09/24/01

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/138,735	Paranhos-Baccala et al.
Examiner	**Art Unit**
Jennifer Graser	1645

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Amendment 12/D, 6/21/01*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 2, 5, 7-27, 29, and 31-35* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, 5, 7-27, 29, and 31-35* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 11

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

1. Acknowledgment and entry of the Amendment submitted 6/21/01, Paper No. 12/D is made. Claims 1, 2, 5, 7-27, 29 and 31-35 are currently pending.

Sequence Compliance

2. The substitute paper and computer readable copies of the sequence listing have been received. It appears that the PTO copied the computer readable copy from application 08/988,242, which is a CIP of 08/480,917, instead of from 08/480,917 as requested by Applicants.

NOTE: A new sequence search using the sequences contained in the substitute computer readable form which was submitted on 6/21/01 has been requested. However, the results from this search were not available at the time of this Office Action. If any prior art references are found once the sequence search results are returned to the Examiner, a Supplemental Office Action will be mailed to Applicants.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 2 and 5, 7-27, 29 and 31-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is vague and confusing because it recites a reagent "comprising a capture probe and a detection probe in accordance with claim 5"; however, claim 5 is drawn to a single probe. Clarification is requested.

Claims 21-24 currently read on genomic or chromosomal DNA from T.cruzi due to the use of the open language "comprising" which allows much more than the specific segments recited. There is no size limitation included in the claim, i.e., no more than 100 nucleotides. At least 30 identical contiguous nucleic acids would be found in isolated chromosomal DNA from *T.cruzi* which was frequently isolated in the prior art to be used in hybridization procedures.

Claims 18, 19 and 27 are vague and indefinite because it fails to state the hybridization conditions. A process which utilizes low stringency conditions would not accurately detect T.cruzi but instead would detect many unrelated organisms as well. The amendment to recite that the "DNA or RNA is exposed to a probe under such conditions that said probe hybridizes to a nucleotide sequence identical or fully complementary..." does not overcome this rejection. It is still unclear what these conditions would be. High stringency conditions would need to be used in order to have an effective assay. The exact hybridization conditions must be recited in the claims. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from

the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed.

Claim 29 is vague and indefinite because it depends from a cancelled claim.

Claim 31 is vague and indefinite because it depends from a cancelled claim.

Claims 21-24 are vague and confusing. It is unclear what the "one segment" in claims 21, 22 and 23 is referring to. These claims are drawn to a synthetic or isolated nucleic acid fragment, i.e, one DNA fragment. How are the two segments in a double stranded DNA different? This is unclear. With respect to claim 24, is this second sequence part of a composition or mixture? The wording of these claims is extremely vague and indefinite.

Claim Rejections - 35 USC § 112-New Matter

5. Claims 5 and 8 and all claims depending from these claims, i.e., claims 7-26, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Support for the new limitation, "**wherein said primer contains *no* more than 100 nucleotides**" could not be found in the instant specification. When providing a new limitation, Applicant should point out to the specific section of the specification by page and line number which provides support for the new limitation.

Claim Rejections - 35 USC § 112-Enablement

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 18, 19, 20, 21, 22, 23, 24, 27, 29 and 31-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The breadth of the instant claims contain nucleotide sequences other than what is specified in the sequence disclosure. The specification states that substitutions, additions, or deletions may be made to the defined sequences; however, the specification provides no guidance as to what nucleotides may be changed without causing a detrimental effect to the protein to be produced or its ability to function as a probe or primer. Further, it is unpredictable as to which nucleotides could be removed and which could be added. Claims 21, 22 and 23 recite sequences which are 85% homologous to 30 contiguous monomers. This allows for a great deal of difference from that which is disclosed in the specification, i.e., much more than 85% variance. These sequences would be up to 70-95% different from SEQ ID NO:1. Sequences with this much deviation would not be able to function as probes or primers. It is unclear what sequence this encompasses and what function it would serve. The breadth of the instant claims contain nucleotide sequences other than what is specified in the sequence disclosure. The specification states that substitutions, additions, or deletions may be made to the defined sequences; however,

the specification provides no guidance as to what nucleotides may be changed without causing a detrimental effect to the probe or primer to be produced. Additionally, 18, 19, 20, 24, 27, 29 and 31-35 are also not enabled as they fail to recite the specific hybridization conditions to be used in the methods. Low stringency conditions would not allow for a successful assay. Applicants have provide no guidance to enable one of ordinary skill in the art how to determine, without undue experimentation, the effects of different nucleotide substitutions and the nature and extent of the changes that can be made. Given the lack of guidance contained in the specification and the unpredictability for determining acceptable nucleotide substitutions, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Response to Applicants' Arguments:

Applicants argue that claims 21-23 encompass percent homology and that one of ordinary skill in the art would be able to determine appropriate sequences by merely routine experimentation for various purposes, such as serving as probes and primers. This has been fully and carefully considered but is not deemed persuasive.

Claims 21, 22 and 23 recite sequences which are 85% homologous to 30 contiguous monomers. This allows for a great deal of difference from that which is disclosed in the specification, i.e., much more than 85% variance. These sequences would be up to 70-**95%** different from SEQ ID NO:1. Sequences with this much deviation would not be able to function as probes or primers. It is unclear what sequence this encompasses and what function it would

serve. The breadth of the instant claims contain nucleotide sequences other than what is specified in the sequence disclosure.

Claim Rejections - 35 USC § 112- Written description

8. Claims 21-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth SEQ ID NO:1, SEQ ID NO: 1 (1232-1825), SEQ ID NO:1 (1232-2207) and equivalent degenerative codon sequences thereof and therefore the written description is not commensurate in scope with the claims drawn to sequences which are 85% homologous to a 30 nucleotide segment and fragments which contain sequences which are complementary to sequences which are antisense which are 5 and 8 nucleotides in length, etc..

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. With the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a

DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Support for antisense and sequences and fragments of varying percent identity is stated. However, no disclosure, beyond the mere mention of these potential sequences is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only an isolated DNA molecule comprising a DNA sequence consisting of nucleotides 1232-1825, 1232-2207 of SEQ ID NO:1 or SEQ ID NO:1 and equivalent degenerative codon sequences thereof, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

Response to Applicants' Arguments:

Applicants argue that a high degree of homology has been claimed (85%) with respect to a defined sequence. They argue that the inventors clearly contemplated such sequences. Applicants further argue that literal support is not needed if the disclosure of the application conveys to the artisan that the inventor had possession at the time of the claimed subject matter. These arguments have been fully and carefully considered but are not deemed persuasive.

Claims 21, 22 and 23 recite sequences which are 85% homologous to 30 contiguous monomers. This allows for a great deal of difference from that which is disclosed in the specification, i.e., much more than 85% variance. These sequences would be up to 70-**95%**

different from SEQ ID NO:1. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required.

9. Applicants' arguments presented on pages 9 and 10 combined with the amendments to the claims were sufficient to overcome the former 102 rejections.

As stated above, if any prior art references are found once the new sequence search results are returned to the Examiner, a Supplemental Office Action will be mailed to Applicants.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 308-4242 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (703) 308-1742. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JEGraser 9/18/01

Jennifer Graser
Primary Examiner
Art Unit 1645